

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2005/003390

International filing date (day/month/year)
04.02.2005

Priority date (day/month/year)
06.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D489/02

Applicant
EURO-CELTIQUE S.A.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Grassi, D

Telephone No. +49 89 2399-8499



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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 38-45(part), 47-65(part), 67-80(part), 85-114 (part), 115-119

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 38-45(part), 47-65(part), 67-80(part), 85-114 (part), 115-119
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-37, 38-45 (part), 46, 47-65 (part), 66, 67-80 (part), 81-84, 85-114 (part)

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2-37, 38-45 (part), 46, 47-65 (part), 66, 67-80 (part), 81-84, 85-114 (part)
	No: Claims	1
Inventive step (IS)	Yes: Claims	
	No: Claims	1-37, 38-45 (part), 46, 47-65 (part), 66, 67-80 (part), 81-84, 85-114 (part)
Industrial applicability (IA)	Yes: Claims	1-37, 38-45 (part), 46, 47-65 (part), 66, 67-80 (part), 81-84, 85-114 (part)
	No: Claims	

2. Citations and explanations

see separate sheet

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Reference is made to the following documents:

- D1: COREY ET AL.: "New and highly effective method for the oxidation of primary and secondary alcohols to carbonyl compounds" J. AMER. CHEM. SOC., vol. 94, no. 21, 1972, pages 7586-7587, (cited in the application)
- D2: US 6 013 796 (cited in the application)
- D3: Xiong, Zhi-Xing et al. "A selective and convenient oxidation of sulfides to sulfoxides with trichloroisocyanuric acid" Synth. Commun., vol 31(2), 2001 245 - 248
- D4: Ulf Tilstam, Hilmar Weinmann, "Trichloroisocyanuric Acid: A Safe and Efficient Oxidant" Organic Process Research & Development, Vol. 6(4) 2002, 384 - 393
- D5: SHIN-ICHI OHSUGI et al.: "New odorless method for the Corey-Kim and Swern oxidations utilizing dodecyl methyl sulfide (Dod-S-Me)" TETRAHEDRON vol. 59, 2003, 8393-8398
- D6: US 6 177 567

Re Item III

The International Searching Authority found multiple (groups of) inventions in this international application. No required additional search fees were paid by the applicant. Consequently, the International Search Report was restricted to the first invention.

Claims relating to inventions in respect of which no International Search Report has been established (i.e. claims: 38-45, 47-65, 67-80, 85-114 [all part], 115-119) need not to be subject of the Written Opinion of the International Searching Authority (Rule 43bis.1(b) PCT in combination with Rule 66.1(e) PCT).

Re Item IV

The International Searching Authority found multiple (groups of) inventions in this international application, the reasons being the following:

D1 represents the closest prior art for claim 1 and generically relates to the oxidation of

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alcohols to ketones or aldehydes by the combined use of a chloramine, dimethyl sulfide and a base (cf. page 7586, scheme, left hand column). The chloramine specified in D1 is N-chlorosuccinimide (a chlorine-containing compound).

The technical problem underlying the present claim 1 (25 and 37) is seen in the provision of an alternative composition for the oxidation of alcohols (or the use thereof).

The claimed solution of the problem resides in a composition comprising a compound of formula R_1SR_2 , trichloroisocyanuric acid (a chlorine-containing compound) and a base.

The technical problem underlying the present claim 62 (38 and 74) is seen in the provision of a reaction composition for the preparation of a compound of formula (II) (or the use thereof).

In this case, the claimed solution of the problem resides in a composition comprising an alcohol of formula (I), a compound of formula R_1SR_2 and a chlorine-containing compound.

The claims 1 and 62 only have the features 'chlorine-containing compound' and 'compound of formula R_1SR_2 ' in common. However, these features are already known from D1 where a composition comprising these compounds is used for the oxidation of alcohols.

Therefore, these claims 1 and 62 do not share a common special technical feature as required by Rule 13.2 PCT, and the present application lacks unity of invention (Rule 13.1 PCT).

Furthermore, the claim 115 relates to an intermediate of formula (III).

The technical problem underlying this claim is seen in the provision of an intermediate in the preparation of morphine derivatives. However, such intermediates are already known from D2 (cf. column 3). Therefore, the claim 115 is also not unitary with either one of claims 1 or 62.

The following different inventions can be identified:

- I Compositions comprising trichloroisocyanuric acid and a compound of formula R_1SR_2 or the use thereof (cf. claims 1-37, 38-45 (part), 46, 47-65 (part), 66, 67-80 (part), 81-

84, 85-114 (part)).

- II Compositions comprising a compound of formula (I), a chlorine-containing compound (not being trichloroisocyanuric acid) and a compound of formula R_1SR_2 or the use thereof (cf. claims 38-45 (part), 47-65 (part), 67-80 (part), 85-114 (part)).
- III Compounds of formula (III) (cf. claims 115-119).

Re Item V

The following considerations only relate to the first invention (i.e. claims 1-37, 38-45 (part), 46, 47-65 (part), 66, 67-80 (part), 81-84, 85-114 (part)).

- 1) The subject-matter of present claim 1 is not new (Article 33(2) PCT).

D3 relates to the oxidation of sulfides with trichloroisocyanuric acid in the presence of a pyridine as base (cf. scheme 1 and compounds 3a and 3c). Consequently, this document discloses compositions comprising these components.

- 2) The subject-matter of claims 1-13 does not involve an inventive step (Article 33(3) PCT).

The closest prior art is represented by D1, generically relating to the oxidation of alcohols to ketones or aldehydes by the combined use of a chloramine, dimethyl sulfide and a base (cf. page 7586, scheme, left hand column, the oxidant is generically represented by $>N-Cl$). In the examples of D1, N-chlorosuccinimide is used as specific chloramine. D1 further mentions that the corresponding reaction can also be carried out by the use of Cl_2 .

The subject-matter of present claim 1 differs from the disclosure of D1 in that another chloramine, namely trichloroisocyanuric acid, is selected. Considering that trichloroisocyanuric acid is a well known alternative to N-chlorosuccinimide (cf. D4), the subject-matter of the present claim 1 represents a selection from the more generic disclosure of D1. Such a selection can only be regarded as inventive, if it presents unexpected effects or properties. However, no such effects or properties are

indicated in the application. Hence, no inventive step is present in the subject-matter of claim 1.

Moreover, the application appears not even to contain experimental evidence that the claimed oxidant composition comprising a compound of formula R_1SR_2 is suitable for the oxidation of alcohols.

The claims 2-13 are obvious with regard to the combination of D1 with D5 (cf. paragraph 2.2).

2.1) The subject-matter of claims 14-24 does not involve an inventive step.

The closest prior art is represented by D6, disclosing the oxidation codeine to give codeinone. D6 proposes several methods for the said oxidation among them a Swern/Moffatt type (DMSO based) oxidation (cf. columns 9 and 10).

The technical problem underlying the present claim 14-24 is seen in the provision of an alternative process. For the time being it cannot be decided whether the problem is solved or not (cf. paragraph 2 and below). Therefore, inventive activity cannot be acknowledged.

D1 teaches that the oxidation of allylic alcohols suffered from side reactions and proposes to apply other mild oxidizing reagents for such alcohols.

Considering the said teaching of D1 and noting that the only example of the present application relating to the preparation of codeinone (example 2) does not apply a sulfide, it is not clear whether the present claims solve the technical problem or not. Therefore, inventive activity cannot be acknowledged.

2.2) In analogy to the claims 1-24, the claims 25-37 do also not involve an inventive step.

2.3) In analogy to the claims 1-24, the claims 38-114 (insofar as relating to the use of trichloroisocyanuric acid) do also not involve an inventive step.

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Remark

In claim 1: a comma after -(C1-C20)alkyl is missing (Article 6 PCT).